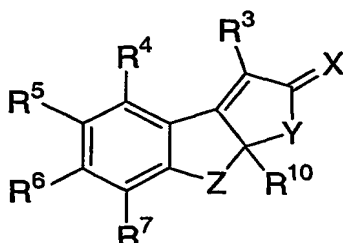


WHAT IS CLAIMED IS:

1. A compound of the formula:



- 5 wherein X is O, N-OR^a, N-NR^aR^b or C₁₋₆ alkylidene, wherein said alkylidene group is unsubstituted or substituted with a group selected from hydroxy, amino, O(C₁₋₄alkyl), NH(C₁₋₄alkyl), or N(C₁₋₄alkyl)₂,
or X represents the following two singly bonded substituents, H and OR^a;
Y is CR¹R², CH₂CR¹R², CH₂CH₂CR¹R² or CH₂CR¹R²CH₂;
10 Z is CR⁸R⁹, CR⁸R⁹CH₂ or CR¹¹=CR¹², and with the proviso that Y can not be CH₂CR¹R² when Z is CR⁸R⁹;
R¹ is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl, wherein said alkyl, alkenyl and alkynyl groups are either unsubstituted or substituted with a group selected from OR^c, SR^c, NR^bR^c, C(=O)R^c, C(=O)CH₂OH, or phenyl, wherein said phenyl group can
15 either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);
R² is hydrogen, hydroxy, iodo, O(C=O)R^c, C(=O)R^c, CO₂R^c, C₁₋₆alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl, wherein said alkyl, alkenyl and alkynyl groups are either unsubstituted
20 or substituted with a group selected from OR^c, SR^c, NR^bR^c, C(=O)R^c, C(=O)CH₂OH, or phenyl, wherein said phenyl group can either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);
25 or R¹ and R², when taken together with the carbon atom to which they are attached, form a carbonyl group;
or R¹ and R², when taken together, form a C₁₋₆ alkylidene group, wherein said alkylidene group is either unsubstituted or substituted with a group selected from hydroxy, O(C₁₋₄alkyl), N(C₁₋₄alkyl)₂ or phenyl, wherein said phenyl group can

either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), NH(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);

5 R³ is hydrogen, fluoro, chloro, bromo, iodo, cyano, nitro, NR^aR^c, OR^a, C(=O)R^a, CO₂R^c, CONR^aR^c, SR^a, S(=O)R^a, SO₂R^a, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, C₅₋₇cycloalkenyl, 4-7 membered heterocycloalkyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, aryl, heteroaryl, arylalkyl or (heteroaryl)alkyl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl and heteroaryl groups are either unsubstituted or independently substituted with 1, 2 or 3 groups selected
10 from fluoro, chloro, bromo, iodo, cyano, OR^a, NR^aR^c, O(C=O)R^a, O(C=O)NR^aR^c, NR^a(C=O)R^c, NR^a(C=O)OR^c, C(=O)R^a, CO₂R^a, CONR^aR^c, CSNR^aR^c, SR^a, S(O)R^a, SO₂R^a, SO₂NR^aR^c, LR^d or MLR^d;

R⁴ is hydrogen, hydroxy or fluoro;

R⁵ is hydrogen, hydroxy, amino, methyl, CF₃, fluoro, chloro or bromo;

15 R⁶ is hydrogen, fluoro, chloro, methyl, amino, OR^a, OR^b, O(C=O)R^c, O(C=O)OR^c, NH(C=O)R^e or NH(C=O)OR^e;

R⁷ is hydrogen, OR^b, NR^bR^c, fluoro, chloro, bromo, iodo, cyano, nitro, C₁₋₆alkyl, C₂₋₆alkenyl, CF₃ or CHF₂;

20 R⁸ and R⁹ are each independently selected from hydrogen, fluoro, chloro, C₁₋₆alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl, or R⁸ and R⁹, when taken together with the carbon atom to which they are attached, form a 3-5 membered cycloalkyl ring, or R⁸ and R⁹, when taken together with the carbon atom to which they are attached, form a carbonyl group;

25 R¹⁰ is hydrogen, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, (cycloalkyl)alkyl, (cycloalkyl)alkenyl, (cycloalkenyl)alkyl, aryl, heteroaryl, arylalkyl or (heteroaryl)alkyl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, (cycloalkyl)alkyl, (cycloalkyl)alkenyl, (cycloalkenyl)alkyl, aryl, heteroaryl, arylalkyl and (heteroaryl)alkyl groups are optionally substituted with a
30 group selected from bromo, iodo, cyano, OR^b, SR^b, C(=O)R^b, 1-3 C₁₋₃alkyl, 1-3 chloro or 1-5 fluoro, or R¹⁰ and R¹, when taken together with the two to four intervening carbon atoms to which they are attached, form a 5-6 membered cycloalkyl or cycloalkenyl ring which is optionally substituted with 1-3 groups independently selected from

oxo, hydroxy, fluoro, chloro, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkylidenyl, C₃₋₆cycloalkyl, (cycloalkyl)alkyl, phenyl, or phenylalkyl, wherein said alkyl, alkenyl, alkynyl, alkylidenyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, and phenylalkyl groups are optionally substituted with a group selected from chloro, bromo, iodo, OR^b, SR^b, C₁₋₃alkyl, C(=O)R^b, or 1-5 fluoro;

R¹¹ is hydrogen, fluoro and C₁₋₄alkyl;

R¹² is hydrogen, fluoro and C₁₋₄alkyl;

R^a is hydrogen, C₁₋₁₀alkyl, and phenyl, wherein said alkyl group is optionally substituted with a group selected from hydroxy, amino, O(C₁₋₄alkyl), NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, phenyl, or 1-5 fluoro, and wherein said phenyl groups can either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);

R^b is hydrogen, C₁₋₁₀alkyl, benzyl or phenyl, wherein said phenyl group can either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);

R^c is hydrogen, C₁₋₁₀alkyl or phenyl, wherein said phenyl group can either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₄alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl); or R^a and R^c, whether or not on the same atom, can be taken together with any attached and intervening atoms to form a 4-7 membered ring;

R^d is NR^bR^c, OR^a, CO₂R^a, O(C=O)R^a, CN, NR^c(C=O)R^b, CONR^aR^c, SO₂NR^aR^c or a 4-9 membered mono- or bi-cyclic N-heterocycloalkyl ring that can be optionally substituted with 1-3 C₁₋₃ alkyl and can be optionally interrupted by O, S, NRC, or C=O;

R^e is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, phenyl or phenylalkyl, wherein said alkyl, alkenyl, or phenyl group can either be unsubstituted or substituted with 1-3 substituents independently selected from C₁₋₃alkyl, OH, O(C₁₋₄alkyl), NH₂, NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, halo, CN, NO₂, CO₂H, CO₂(C₁₋₄alkyl), C(O)H or C(O)(C₁₋₄alkyl);

L is CR^bR^c , C_{2-6} alkylene or C_{2-6} alkenylene, wherein said alkylene and alkenylene linkers can be optionally interrupted by O, S, or NR^c ;

M is O, S, NR^c , $\text{C}=\text{O}$, $\text{O}(\text{C}=\text{O})$, $(\text{C}=\text{O})\text{O}$, $\text{NR}^c(\text{C}=\text{O})$ or $(\text{C}=\text{O})\text{NR}^c$;
or a pharmaceutically acceptable salt thereof.

5

2. The compound of Claim 1 wherein X is O or N-OR^a ;

Y is CR^1R^2 , $\text{CH}_2\text{CR}^1\text{R}^2$ or $\text{CH}_2\text{CH}_2\text{CR}^1\text{R}^2$;

Z is CR^8R^9 or CH_2CH_2 , with the proviso that Y can not be $\text{CH}_2\text{R}^1\text{R}^2$ when Z is CR^8R^9 ;

R^1 is hydrogen or C_{1-6} alkyl, wherein said group is either unsubstituted or substituted with a group selected from OR^c or $\text{C}(=\text{O})\text{R}^c$;

10

R^2 is hydrogen, hydroxy or C_{1-6} alkyl, wherein said alkyl group is either unsubstituted or substituted with a group selected from OR^c or $\text{C}(=\text{O})\text{R}^c$;

R^3 is chloro, bromo, iodo, cyano, CO_2R^c , C_{1-10} alkyl, C_{3-7} cycloalkyl, aryl or heteroaryl, wherein said alkyl, cycloalkyl, aryl and heteroaryl groups are either unsubstituted or independently substituted with 1, 2 or 3 groups selected from fluoro, chloro, bromo, cyano, OR^a , CO_2R^a , LR^d or MLR^d ;

15

R^4 is hydrogen or fluoro;

R^5 is hydrogen, hydroxy, fluoro, chloro or bromo;

R^6 is hydrogen, fluoro, amino, OR^a or $\text{O}(\text{C}=\text{O})\text{R}^c$;

20

R^7 is hydrogen, fluoro, chloro, bromo or C_{1-6} alkyl;

R^8 and R^9 are each independently selected from hydrogen, fluoro, chloro or C_{1-6} alkyl, or R^8 and R^9 , when taken together with the carbon atom to which they are attached, form a carbonyl group;

R^{10} is C_{1-10} alkyl, C_{2-10} alkenyl, C_{3-6} cycloalkyl or (cycloalkyl)alkyl, wherein said alkyl, alkenyl, cycloalkyl, and (cycloalkyl)alkyl groups are optionally substituted with a group selected from bromo, SR^b , 1-3 chloro or 1-5 fluoro;

25

or a pharmaceutically acceptable salt thereof.

3. The compound of Claim 2 wherein X is O or N-OH ;

30 Y is CR^1R^2 or $\text{CH}_2\text{CH}_2\text{CR}^1\text{R}^2$;

Z is CH_2 or CH_2CH_2 ;

R^1 is hydrogen or C_{1-3} alkyl;

R^2 is hydrogen, hydroxy or C_{1-3} alkyl;

R³ is chloro, bromo, cyano, C₁₋₁₀alkyl, C₃₋₇cycloalkyl, aryl or heteroaryl, wherein said alkyl, cycloalkyl, aryl, and heteroaryl groups are either unsubstituted or independently substituted with 1, 2 or 3 groups selected from fluoro, chloro, cyano, OR^a, LR^d or MLR^d;

- 5 R⁴ is hydrogen;
 R⁵ is hydrogen or fluoro;
 R⁶ is OR^a or O(C=O)R^c;
 R⁷ is hydrogen, chloro or methyl;
 R⁸ and R⁹ are each hydrogen, or R⁸ and R⁹, when taken together with the carbon atom to which
 10 they are attached, form a carbonyl group;
 R¹⁰ is C₁₋₁₀alkyl or (cycloalkyl)alkyl, wherein said alkyl and (cycloalkyl)alkyl groups are unsubstituted or substituted with 1-5 fluoro;
 or a pharmaceutically acceptable salt thereof.

- 15 4. The compound of Claim 3 wherein X is O;
 Y is CH₂ or CH₂CH₂CH₂;
 R¹ is hydrogen;
 R² is hydrogen;
 R³ is chloro, bromo, cyano, methyl, ethyl, trifluoromethyl, cyclopropyl, phenyl, furyl or thienyl;
 20 R⁶ is hydroxy;
 R⁸ and R⁹ are each hydrogen;
 an or a pharmaceutically acceptable salt thereof.

5. The compound of Claim 1 selected from the group consisting of:
 25 3-bromo-8a-butyl-6-hydroxy-8,8a-dihydrocyclopenta[*a*]inden-2(1*H*)-one;
 (*rac*)-(1*S*,8*aR*)-3-bromo-8a-butyl-6-hydroxy-1-propyl-8,8a-dihydrocyclopenta[*a*]inden-2(1*H*)-one;
 1,3a-diethyl-7-hydroxy-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 3a-butyl-7-hydroxy-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 30 1,6-dibromo-3a-butyl-7-hydroxy-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 1-bromo-3a-butyl-7-hydroxy-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 6-bromo-3a-butyl-7-hydroxy-1-methyl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 3a-butyl-7-hydroxy-1,6-dimethyl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;
 3a-butyl-7-hydroxy-1-methyl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalen-2-one;

- 1-bromo-3a-butyl-6-chloro-8-fluoro-7-hydroxy-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 10a-butyl-7-hydroxy-1,9,10,10a-tetrahydro-3(2H)-phenanthrenone;
- 4-bromo-10a-butyl-7-hydroxy-1,9,10,10a-tetrahydro-3(2H)-phenanthrenone;
- 5 9a-butyl-2-hydroxy-5-methyl-8,9,9a,10-tetrahydrobenzo[a]azulen-6(7H)-one;
- 1-bromo-7-hydroxy-3a-methyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 7-hydroxy-1,3a-dimethyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 1,6-dibromo-7-hydroxy-3a-methyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 6-bromo-7-hydroxy-1,3a-dimethyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 10 1-bromo-3a-ethyl-7-hydroxy-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 3a-ethyl-7-hydroxy-1-methyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 1,6-dibromo-3a-ethyl-7-hydroxy-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 1-bromo-7-hydroxy-3a-propyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 7-hydroxy-1-methyl-3a-propyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 15 1,6-dibromo-7-hydroxy-3a-propyl-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 1-bromo-6-chloro-3a-ethyl-7-hydroxy-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- 1-bromo-3a-butyl-6-chloro-7-hydroxy-3,3a,4,5-tetrahydro-2H-cyclopenta[a]naphthalen-2-one;
- and the pharmaceutically acceptable salts thereof.

- 20 6. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.
7. A pharmaceutical composition made by combining a compound according to Claim 1 and a pharmaceutically acceptable carrier.
- 25 8. A process for making a pharmaceutical composition comprising combining a compound according to Claim 1 and a pharmaceutically acceptable carrier.
9. A method of eliciting an estrogen receptor modulating effect in a mammal
- 30 in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.
10. The method according to Claim 9 wherein the estrogen receptor modulation effect is an estrogen receptor agonizing effect.

11. The method according to Claim 10 wherein the estrogen receptor agonizing effect is an ER β receptor agonizing effect.

5 12. A method of treating or preventing a disease in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1, wherein said disease is: bone loss, bone fractures, osteoporosis, metastatic bone disease, Paget's disease, periodontal disease, cartilage degeneration, endometriosis, uterine fibroid disease, hot flashes, increased levels of LDL cholesterol, cardiovascular disease, impairment of
10 cognitive functioning, cerebral degenerative disorders, restenosis, gynecomastia, vascular smooth muscle cell proliferation, obesity, incontinence, anxiety, depression, perimenopausal depression, post-partum depression, premenstrual syndrome, manic depression, anxiety, dementia, obsessive compulsive behavior, attention deficit disorder, sleep disorders, irritability, impulsivity, anger management, multiple sclerosis and Parkinson's disease or an estrogen dependent cancer.

15 13. The method of Claim 12 wherein the disease is hot flashes.

14. The method of Claim 12 wherein the disease is depression.

20 15. A method of treating or preventing an estrogen dependent cancer in a mammal in need thereof by administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

25 16. A pharmaceutical composition comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate; a cathepsin K inhibitor; an estrogen; an estrogen receptor modulator; an androgen receptor modulator; an inhibitor of osteoclast proton ATPase; an inhibitor of HMG-CoA reductase; an integrin receptor antagonist; an osteoblast anabolic agent; calcitonin; Vitamin D; a synthetic Vitamin D analogue; or a selective serotonin reuptake inhibitor; or a pharmaceutically acceptable salt or mixture thereof.

30 17. A method of treating hot flashes comprising administering to a mammal in need thereof a compound of Claim 1 and another agent selected from: an organic bisphosphonate; a cathepsin K inhibitor; an estrogen; an estrogen receptor modulator; an androgen receptor modulator; an inhibitor of osteoclast proton ATPase; an inhibitor of HMG-

CoA reductase; an integrin receptor antagonist; an osteoblast anabolic agent; calcitonin; Vitamin D; a synthetic Vitamin D analogue; or a selective serotonin reuptake inhibitor; or a pharmaceutically acceptable salt or mixture thereof.

5 18. A method of treating depression comprising administering to a mammal in
need thereof a compound of Claim 1 and another agent selected from: an organic
bisphosphonate; a cathepsin K inhibitor; an estrogen; an estrogen receptor modulator; an
androgen receptor modulator; an inhibitor of osteoclast proton ATPase; an inhibitor of HMG-
10 CoA reductase; an integrin receptor antagonist; an osteoblast anabolic agent; calcitonin; Vitamin
D; a synthetic Vitamin D analogue; or a selective serotonin reuptake inhibitor; or a
pharmaceutically acceptable salt or mixture thereof.

15 19. A method of treating an estrogen dependent cancer comprising
administering to a mammal in need thereof a compound of Claim 1 and another agent selected
from: an organic bisphosphonate; a cathepsin K inhibitor; an estrogen; an estrogen receptor
modulator; an androgen receptor modulator; an inhibitor of osteoclast proton ATPase; an
inhibitor of HMG-CoA reductase; an integrin receptor antagonist; an osteoblast anabolic agent;
calcitonin; Vitamin D; a synthetic Vitamin D analogue; or a selective serotonin reuptake
inhibitor; or a pharmaceutically acceptable salt or mixture thereof.

20 20. A method of lowering cholesterol comprising administering to a mammal
in need thereof a compound of Claim 1 and another agent selected from: an organic
bisphosphonate; a cathepsin K inhibitor; an estrogen; an estrogen receptor modulator; an
androgen receptor modulator; an inhibitor of osteoclast proton ATPase; an inhibitor of HMG-
25 CoA reductase; an integrin receptor antagonist; an osteoblast anabolic agent; calcitonin; Vitamin
D; a synthetic Vitamin D analogue; or a selective serotonin reuptake inhibitor; or a
pharmaceutically acceptable salt or mixture thereof.